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IN THE SPECIFICATION:

At page 9, please replace paragraphs [035] through [037] with the following text:

Figure 4 depicts a BLAST alignment of human 80090 with a consensus amino acid sequence derived from a ProDomain No. PD313476, "CG4435" (Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 40-217 of the 229 amino acid consensus sequence (SEQ ID NO:17), while the upper amino acid sequence corresponds to the "CG4435" domain of human 80090, amino acid residues 89-265 of SEQ ID NO:2.

Figure 5 depicts a BLAST alignment of human 80090 with a consensus amino acid sequence derived from a ProDomain No. PD002778, "Transferase fucosyltransferase glycosyltransferase alpha-12-fucosyltransferase galactoside transmembrance glycoprotein 3-L- signal-anchor golgi" (Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 62-200 of the 227 amino acid consensus sequence (SEQ ID NO:18), while the upper amino acid sequence corresponds to the "Transferase fucosyltransferase glycosyltransferase alpha-12-fucosyltransferase galactoside transmembrance glycoprotein 3-L- signal-anchor golgi" domain of human 80090, amino acid residues 221-367 of SEQ ID NO:2.

Figure 6 depicts a BLAST alignment of human 80090 with a consensus amino acid sequence derived from a ProDomain No. PD323544, "CG9169" (Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 129-424 of the 445 amino acid consensus sequence (SEQ ID NO:19), while the upper amino acid sequence corresponds to the "CG9169" domain of human 80090, amino acid residues 90-390 of SEQ ID NO:2.

At pages 10 through 11, please replace paragraphs [0041-0043] with the following text:

Figure 10 depicts a BLAST alignment of human 52874 with a consensus amino acid sequence derived from a ProDomain No. PD032606, "Receptor neurotensin coupled G-protein type transmembrane lipoprotein levocabastine- palmitate phosphorylation" (Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 12-76 of the 84 amino acid consensus sequence (SEQ ID NO:22), while the upper amino acid sequence corresponds to the "Receptor neurotensin coupled G-protein type transmembrane lipoprotein levocabastine- palmitate phosphorylation" domain of human 52874, amino acid residues 253-320 of SEQ ID NO:5.

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Figure 11 depicts a BLAST alignment of human 52874 with a consensus amino acid sequence derived from a ProDomain No. PD128109, "Similar somatostatin receptors" (Release 2001.1; Corpet *et al. (1999), Nucl. Acids Res. 27:263-267* and Gouzy *et al. (1999) Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 160-267 of the 305 amino acid consensus sequence (SEQ ID NO:23), while the upper amino acid sequence corresponds to the "Similar somatostatin receptors" domain of human 52874, amino acid residues 208-316 of SEQ ID NO:5.

Figure 12 depicts a BLAST alignment of human 52874 with a consensus amino acid sequence derived from a ProDomain No. PD145471, "C01G12.7" (Release 2001.1; Corpet *et al. (1999), Nucl. Acids Res. 27:263-267* and Gouzy *et al. (1999) Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 115-298 of the 599 amino acid consensus sequence (SEQ ID NO:24), while the upper amino acid sequence corresponds to the "C01G12.7" domain of human 52874, amino acid residues 16-192 of SEQ ID NO:5.

At pages 11 through 12, please replace paragraphs [0047-0050] with the following text:

Figure 16 depicts a BLAST alignment of human 52880 with a consensus amino acid sequence derived from a ProDomain No. PD310793, "Receptor orphan GPR26 protein-coupled" (Release 2001.1; Corpet *et al. (1999), Nucl. Acids Res. 27:263-267* and Gouzy *et al. (1999) Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 2-183 of the 205 amino acid consensus sequence (SEQ ID NO:26), while the upper amino acid sequence corresponds to the "Receptor orphan GPR26 protein-coupled" domain of human 52880, amino acid residues 134-315 of SEQ ID NO:8.

Figure 17 depicts a BLAST alignment of human 52880 with a consensus amino acid sequence derived from a ProDomain No. PD155019, "Receptor type hypocretin EG:22E5.10 EG:22E5.11 transmembrane coupled orexin G-protein" (Release 2001.1; Corpet *et al. (1999), Nucl. Acids Res. 27:263-267* and Gouzy *et al. (1999) Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 28-184 of the 227 amino acid consensus sequence (SEQ ID NO:27), while the upper amino acid sequence corresponds to the "Receptor type hypocretin EG:22E5.10 EG:22E5.11 transmembrane coupled orexin G-protein" domain of human 52880, amino acid residues 175-321 of SEQ ID NO:8.

Figure 18 depicts a BLAST alignment of human 52880 with a consensus amino acid sequence derived from a ProDomain No. PD032094, "Receptor acid lysophosphatidic high-affinity homolog transmembrane novel rhodopsin similar" (Release 2001.1; Corpet *et al. (1999), Nucl. Acids Res. 27:263-267* and Gouzy *et al. (1999) Computers and Chemistry* 23:333-340

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~~http://www.toulouse.inra.fr/prodom.html~~). The lower sequence is amino acid residues 24-183 of the 202 amino acid consensus sequence (SEQ ID NO:28), while the upper amino acid sequence corresponds to the "Receptor acid lysophosphatidic high-affinity homolog transmembrane novel rhodopsin similar" domain of human 52880, amino acid residues 171-322 of SEQ ID NO:8.

Figure 19 depicts a BLAST alignment of human 52880 with a consensus amino acid sequence derived from a ProDomain No. PD322057, "NT2RM2000452 FLJ10317 Fis cDNA" (Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 ~~http://www.toulouse.inra.fr/prodom.html~~). The lower sequence is amino acid residues 7-99 of the 388 amino acid consensus sequence (SEQ ID NO:29), while the upper amino acid sequence corresponds to the "NT2RM2000452 FLJ10317 Fis cDNA" domain of human 52880, amino acid residues 221-329 of SEQ ID NO:8.

At page 13, please replace paragraphs [0054] with the following text:

Figure 23 depicts a BLAST alignment of human 63497 with a consensus amino acid sequence derived from a ProDomain No. PD009900, "Receptor pheromone G-protein vomeronasal coupled M24 VN1 VN3 VN2 VN4" (Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 ~~http://www.toulouse.inra.fr/prodom.html~~). The lower sequence is amino acid residues 5-264 of the 274 amino acid consensus sequence (SEQ ID NO:31), while the upper amino acid sequence corresponds to the "Receptor pheromone G-protein vomeronasal coupled M24 VN1 VN3 VN2 VN4" domain of human 63497, amino acid residues 36-295 of SEQ ID NO:11.

At pages 14 through 15, please replace paragraphs [0058-0060] with the following text:

Figure 27 depicts a BLAST alignment of human 33425 with a consensus amino acid sequence derived from a ProDomain No. PD301916, "Similar NT2RM2000363 cluster Fis FLJ10312 weakly cDNA breakpoint" (Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 ~~http://www.toulouse.inra.fr/prodom.html~~). The lower sequence is amino acid residues 1-103 of the 153 amino acid consensus sequence (SEQ ID NO:33), while the upper amino acid sequence corresponds to the "Similar NT2RM2000363 cluster Fis FLJ10312 weakly cDNA breakpoint" domain of human 33425, amino acid residues 516-608 of SEQ ID NO:14.

Figure 28 depicts a BLAST alignment of human 33425 with a consensus amino acid sequence derived from a ProDomain No. PD000780, "GTPase activating similar GTPase-activating activation domain Fis zinc cDNA subunit" (Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 ~~http://www.toulouse.inra.fr/prodom.html~~).

The lower sequence is amino acid residues 16-118 of the 161 amino acid consensus sequence (SEQ ID NO:34), while the upper amino acid sequence corresponds to the "GTPase activating similar GTPase-activating activation domain Fis zinc cDNA subunit" domain of human 33425, amino acid residues 390-486 of SEQ ID NO:14.

Figure 29 depicts a BLAST alignment of human 33425 with a consensus amino acid sequence derived from a ProDomain No. PD215173, "RLIP" (Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). The lower sequence is amino acid residues 96-185 of the 186 amino acid consensus sequence (SEQ ID NO:35), while the upper amino acid sequence corresponds to the "RLIP" domain of human 33425, amino acid residues 399-488 of SEQ ID NO:14.

At page 16, please replace paragraph [0064] with the following text:

For general information regarding PFAM identifiers, PS prefix, and PF prefix domain identification numbers, refer to Sonnhammer et al. (1997) *Protein* 28:405-420 and http://www.pse.edu/general/software/packages/pfam/pfam.html.

At pages 17 through 18, please replace paragraphs [0071-0072] with the following text:

To identify the presence of a "fucosyltransferase" domain in an 80090 protein sequence, and make the determination that a polypeptide or protein of interest has a particular profile, the amino acid sequence of the protein can be searched against a database of HMMs (e.g., the Pfam database, release 2.1) using the default parameters (http://www.sanger.ac.uk/Software/Pfam/HMM_search). For example, the hmmsf program, which is available as part of the HMMER package of search programs, is a family specific default program for MILPAT0063, and a score of 15 is the default threshold score for determining a hit. Alternatively, the threshold score for determining a hit can be lowered (e.g., to 8 bits). A description of the Pfam database can be found in Sonhammer et al. (1997) Proteins 28(3):405-420, and a detailed description of HMMs can be found, for example, in Gribskov et al.(1990) Meth. Enzymol. 183:146-159; Gribskov et al.(1987) Proc. Natl. Acad. Sci. USA 84:4355-4358; Krogh et al.(1994) J. Mol. Biol. 235:1501-1531; and Stultz et al.(1993) Protein Sci. 2:305-314, the contents of which are incorporated herein by reference. A search was performed against the HMM database resulting in the identification of a fucosyltransferase domain in the amino acid sequence of human 80090 at about residues 35-395 of SEQ ID NO:2 (see Figure 1).

An 80090 polypeptide can include a fucosyltransferase domain or regions homologous with a fucosyltransferase domain. As used herein, the fucosyltransferase domain includes an amino acid

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sequence of about 200-500 amino acid residues in length. Preferably, an fucosyltransferase protein

domain includes at least about 250-450 amino acids, more preferably about 300-400 amino acids, or

about 350-375 amino acids. The fucosyltransferase domain (HMM) has been assigned the PFAM

Accession PF00852 (http://pfam.wustl.edu/). An alignment of the fucosyltransferase domain (amino

acids 35-395 of SEQ ID NO:2) of human 80090 with a consensus amino acid sequence derived from a

hidden Markov model is depicted in Figure 3.

At pages 18 through 19, please replace paragraphs [0075-0078] with the following text:

A BLAST search was performed against the HMM database resulting in the identification of a

region homologous to ProDom family PD313476("CG4435" SEQ ID NO:17, ProDomain Release

2001.1; Corpet <u>et al.</u> (1999), <u>Nucl. Acids Res.</u> 27:263-267 and Gouzy <u>et al.</u> (1999) <u>Computers and</u>

<u>Chemistry</u> 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "CG4435" domain

(amino acids 89-265 of SEQ ID NO:2) of human 80090 with a consensus amino acid sequence (SEQ ID

NO:17) derived from a hidden Markov model is depicted in Figure 4. The consensus sequence for SEQ

ID NO:17 is 42% identical over amino acids 89-265 of SEQ ID NO:2 as shown in Figure 4.

A BLAST search was performed against the HMM database resulting in the identification of a

region homologous to ProDom family PD002778("Transferase fucosyltransferase glycosyltransferase

alpha-12-fucosyltransferase galactoside transmembrance glycoprotein 3-L- signal-anchor golgi" SEQ ID

NO:18, ProDomain Release 2001.1; Corpet <u>et al.</u> (1999), <u>Nucl. Acids Res.</u> 27:263-267 and Gouzy <u>et al.</u>

(1999) <u>Computers and Chemistry</u> 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment

of the "Transferase fucosyltransferase glycosyltransferase alpha-12-fucosyltransferase galactoside

transmembrance glycoprotein 3-L- signal-anchor golgi" domain (amino acids 221-367 of SEQ ID NO:2)

of human 80090 with a consensus amino acid sequence (SEQ ID NO:18) derived from a hidden Markov

model is depicted in Figure 5. The consensus sequence for SEQ ID NO:18 is 36% identical over amino

acids 221-367 of SEQ ID NO:2 as shown in Figure 5.

A BLAST search was performed against the HMM database resulting in the identification of a

region homologous to ProDom family PD323544("CG9169" SEQ ID NO:19, ProDomain Release

2001.1; Corpet <u>et al.</u> (1999), <u>Nucl. Acids Res.</u> 27:263-267 and Gouzy <u>et al.</u> (1999) <u>Computers and</u>

<u>Chemistry</u> 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "CG9169" domain

(amino acids 90-390 of SEQ ID NO:2) of human 80090 with a consensus amino acid sequence (SEQ ID

NO:19) derived from a hidden Markov model is depicted in Figure 6. The consensus sequence for SEQ

ID NO:19 is 24% identical over amino acids 90-390 of SEQ ID NO:2 as shown in Figure 6.

A BLAST search was performed against the HMM database resulting in the identification of a

region homologous to ProDom family PD323544("CG9169" SEQ ID NO:19, ProDomain Release

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2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 ~~http://www.toulouse.inra.fr/prodom.html~~). An alignment of the "CG9169" domain (amino acids 90-390 of SEQ ID NO:2) of human 80090 with a consensus amino acid sequence (SEQ ID NO:19) derived from a hidden Markov model is depicted in Figure 6. The consensus sequence for SEQ ID NO:19 is 24% identical over amino acids 90-390 of SEQ ID NO:2 as shown in Figure 6.

At page 23, please replace paragraphs [0092] with the following text:

For general information regarding PFAM identifiers, PS prefix, and PF prefix domain identification numbers, refer to Sonnhammer et al. (1997) *Protein* 28:405-420 ~~and http://www.psc.edu/general/software/packages/pfam/pfam.html~~.

At page 24, please replace paragraph [0098] with the following text:

For general information regarding PFAM identifiers, PS prefix, and PF prefix domain identification numbers, refer to Sonnhammer et al. (1997) *Protein* 28:405-420 ~~and http://www.psc.edu/general/software/packages/pfam/pfam.html~~.

At page 26, please replace paragraphs [0104] with the following text:

For general information regarding PFAM identifiers, PS prefix, and PF prefix domain identification numbers, refer to Sonnhammer et al. (1997) *Protein* 28:405-420 ~~and http://www.psc.edu/general/software/packages/pfam/pfam.html~~.

At pages 27 through 28, please replace paragraph [0108] with the following text:

As used herein, the term "G protein-coupled receptor" or "GPCR" refers to a family of proteins that preferably comprise an N-terminal extracellular domain, seven transmembrane domains (also referred to as membrane-spanning domains), three extracellular domains (also referred to as extracellular loops), three cytoplasmic domains (also referred to as cytoplasmic loops), and a C-terminal cytoplasmic domain (also referred to as a cytoplasmic tail). Members of the GPCR family also share certain conserved amino acid residues, some of which have been determined to be critical to receptor function and/or G protein signaling. For example, GPCRs usually contain the following features including a conserved asparagine residue in the first transmembrane domain. ~~An alignment of the~~

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~~transmembrane domains of 44 representative GPCRs can be found at~~
~~http://mgdkk1.nidll.nih.gov:8000/extended.html.~~

At pages 31 through 32, please replace paragraphs [0117-0118] with the following text:

To identify the presence of a 7 transmembrane receptor profile in a 52874, 52880, or 63497 receptor, and make the determination that a polypeptide or protein of interest has a particular profile, the amino acid sequence of the protein can be searched against the Pfam database of HMMs (*e.g.*, the Pfam database, release 2.1) using the default parameters ~~(http://www.sanger.ac.uk/Software/Pfam/HMM_search)~~. For example, the hmmsf program, which is available as part of the HMMER package of search programs, is a family specific default program for PF00001 and a score of 15 is the default threshold score for determining a hit. Alternatively, the threshold score for determining a hit can be lowered (*e.g.*, to 8 bits). A description of the Pfam database can be found in Sonhammer *et al.* (1997) *Proteins* 28:405-420 and a detailed description of HMMs can be found, for example, in Gribskov *et al.* (1990) *Meth. Enzymol.* 183:146-159; Gribskov *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:4355-4358; Krogh *et al.* (1994) *J. Mol. Biol.* 235:1501-1531; and Stultz *et al.* (1993) *Protein Sci.* 2:305-314, the contents of which are incorporated herein by reference. Alternatively, the seven transmembrane domain can be predicted based on stretches of hydrophobic amino acids forming α-helices (SOUSI server). For example, using a SOUSI server, two 7 TM receptor domain profiles were identified in the amino acid sequence of SEQ ID NO:5 (*e.g.*, amino acids 40-120 and 142-293 of SEQ ID NO:5), one 7TM receptor domain profile in the amino acid sequence of SEQ ID NO: 8 (*e.g.*, amino acids 22-294 of SEQ ID NO:8), and one 7TM receptor domain profile in the amino acid sequence of SEQ ID NO:11 (*e.g.*, amino acids 189-243 of SEQ ID NO:11). Accordingly, 52874, 52880, or 63497 proteins having at least 50-60% homology, preferably about 60-70%, more preferably about 70-80%, or about 80-90% homology with the 7 transmembrane receptor profile of human 52874, 52880, or 63497 are within the scope of the invention.

In one embodiment, a 52874, 52880, or 63497 protein includes at least one "7 transmembrane receptor" domain or regions homologous with a "7 transmembrane receptor" domain. As used herein, the term "7 transmembrane receptor" domain includes an amino acid sequence having at least about 10-350 amino acid residues in length and having a bit score for the alignment of the sequence to the 7tm_1 family Hidden Markov Model (HMM) of at least 8. Preferably, a "7 transmembrane receptor family" domain includes at least about 50-350 amino acid residues, more preferably about 75-300 amino acid residues, or at least about 80-280 amino acids in length and having a bit score for the alignment of the sequence to the "7 transmembrane receptor family" domain (HMM) of at least 12 or greater. The "7 transmembrane receptor family" domain (HMM) has been assigned the PFAM Accession PF00001

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(http://pfam.wustl.edu/cgi-bin/getdesc?name=7tm_1). An alignment of the "7 transmembrane receptor family" domain (amino acids 40-120 and 142-293 of SEQ ID NO:5, 22-294 of SEQ ID NO:8 and 189-243 of SEQ ID NO:11) of human 52874, 52880, or 63497 with a consensus amino acid sequence derived from a hidden Markov model is depicted in Figures 9A-B, 15, and 22.

At pages 33 through 36, please replace paragraphs [0122-0129] with the following text:

A BLAST search was performed against the HMM database resulting in the identification of regions homologous to ProDom family PD032606("Receptor neurotensin coupled G-protein type transmembrane lipoprotein levocabastine- palmitate phosphorylation" SEQ ID NO:22, ProDomain Release 2001.1; Corpet _et al. (1999), Nucl. Acids Res._ 27:263-267 and Gouzy _et al. (1999) Computers and Chemistry_ 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "Receptor neurotensin coupled G-protein type transmembrane lipoprotein levocabastine- palmitate phosphorylation" domain (amino acids 253-320 of SEQ ID NO:5) of human 52874 with consensus amino acid sequences (SEQ ID NO:22) derived from a hidden Markov model is depicted in Figure 10. The consensus sequence for SEQ ID NO:22 is 33% identical over amino acids 253-320 of SEQ ID NO:5 as shown in Figure 10.

A BLAST search was performed against the HMM database resulting in the identification of regions homologous to ProDom family PD128109("Similar somatostatin receptors" SEQ ID NO:23, ProDomain Release 2001.1; Corpet _et al. (1999), Nucl. Acids Res._ 27:263-267 and Gouzy _et al. (1999) Computers and Chemistry_ 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "Similar somatostatin receptors" domain (amino acids 208-316 of SEQ ID NO:5) of human 52874 with consensus amino acid sequences (SEQ ID NO:23) derived from a hidden Markov model is depicted in Figure 11. The consensus sequence for SEQ ID NO:23 is 24% identical over amino acids 208-316 of SEQ ID NO:5 as shown in Figure 11.

A BLAST search was performed against the HMM database resulting in the identification of regions homologous to ProDom family PD145471("C01G12.7" SEQ ID NO:24, ProDomain Release 2001.1; Corpet _et al. (1999), Nucl. Acids Res._ 27:263-267 and Gouzy _et al. (1999) Computers and Chemistry_ 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "C01G12.7" domain (amino acids 16-192 of SEQ ID NO:5) of human 52874 with consensus amino acid sequences (SEQ ID NO:24) derived from a hidden Markov model is depicted in Figure 12. The consensus sequence for SEQ ID NO:24 is 20% identical over amino acids 16-192 of SEQ ID NO:5 as shown in Figure 12.

A BLAST search was performed against the HMM database resulting in the identification of regions homologous to ProDom family PD310793("Receptor orphan GPR26 protein-coupled" SEQ ID NO:26, ProDomain Release 2001.1; Corpet _et al. (1999), Nucl. Acids Res._ 27:263-267 and Gouzy _et al. (1999) Computers and Chemistry_ 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment

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of the "Receptor orphan GPR26 protein-coupled" domain (amino acids 134-315 of SEQ ID NO:8) of human 52880 with consensus amino acid sequences (SEQ ID NO:26) derived from a hidden Markov model is depicted in Figure 16. The consensus sequence for SEQ ID NO:26 is 51% identical over amino acids 134-315 of SEQ ID NO:8 as shown in Figure 16.

A BLAST search was performed against the HMM database resulting in the identification of regions homologous to ProDom family PD155019("Receptor type hypocretin EG:22E5.10 EG:22E5.11 transmembrane coupled orexin G-protein" SEQ ID NO:27, ProDomain Release 2001.1; Corpet _et al._ (1999), _Nucl. Acids Res._ 27:263-267 and Gouzy _et al._ (1999) _Computers and Chemistry_ 23:333-340 · http://www.toulouse.inra.fr/prodom.html). An alignment of the "Receptor type hypocretin EG:22E5.10 EG:22E5.11 transmembrane coupled orexin G-protein" domain (amino acids 175-321 of SEQ ID NO:8) of human 52880 with consensus amino acid sequences (SEQ ID NO:27) derived from a hidden Markov model is depicted in Figure 17. The consensus sequence for SEQ ID NO:27 is 23% identical over amino acids 175-321 of SEQ ID NO:8 as shown in Figure 17.

A BLAST search was performed against the HMM database resulting in the identification of regions homologous to ProDom family PD032094("Receptor acid lysophosphatidic high-affinity homolog transmembrane novel thodopsin similar" SEQ ID NO:28, ProDomain Release 2001.1; Corpet _et al._ (1999), _Nucl. Acids Res._ 27:263-267 and Gouzy _et al._ (1999) _Computers and Chemistry_ 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "Receptor acid lysophosphatidic high-affinity homolog transmembrane novel thodopsin similar" domain (amino acids 171-322 of SEQ ID NO:8) of human 52880 with consensus amino acid sequences (SEQ ID NO:28) derived from a hidden Markov model is depicted in Figure 18. The consensus sequence for SEQ ID NO:28 is 22% identical over amino acids 171-322 of SEQ ID NO:8 as shown in Figure 18.

A BLAST search was performed against the HMM database resulting in the identification of regions homologous to ProDom family PD322057("NT2RM2000452 FLJ10317 Fis cDNA" SEQ ID NO:29, ProDomain Release 2001.1; Corpet _et al._ (1999), _Nucl. Acids Res._ 27:263-267 and Gouzy _et al._ (1999) _Computers and Chemistry_ 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "NT2RM2000452 FLJ10317 Fis cDNA" domain (amino acids 221-329 of SEQ ID NO:8) of human 52880 with consensus amino acid sequences (SEQ ID NO:29) derived from a hidden Markov model is depicted in Figure 19. The consensus sequence for SEQ ID NO:29 is 30% identical over amino acids 221-329 of SEQ ID NO:8 as shown in Figure 19.

A BLAST search was performed against the HMM database resulting in the identification of regions homologous to ProDom family PD009900("Receptor pheromone G-protein vomeronasal coupled M24 VN1 VN3 VN2 VN4" SEQ ID NO:31, ProDomain Release 2001.1; Corpet _et al._ (1999), _Nucl. Acids Res._ 27:263-267 and Gouzy _et al._ (1999) _Computers and Chemistry_ 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "Receptor pheromone G-protein

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vomeronasal coupled M24 VN1 VN3 VN2 VN4" domain (amino acids 36-295 of SEQ ID NO:11) of human 63497 with consensus amino acid sequences (SEQ ID NO:31) derived from a hidden Markov model is depicted in Figure 23. The consensus sequence for SEQ ID NO:31 is 34% identical over amino acids 36-295 of SEQ ID NO:11 as shown in Figure 23.

At page 42, please replace paragraph [0149] with the following text:

For general information regarding PFAM identifiers, PS prefix, and PF prefix domain identification numbers, refer to Sonnhammer et al. (1997) *Protein* 28:405-420 ~~and http://www.psc.edu/general/ software/packages/pfam/pfam.html~~.

At pages 43 through 44, please replace paragraph [0157] with the following text:

As used herein, the term "rhoGAP domain" includes an amino acid sequence of about 50-300 amino acid residues in length and having a bit score for the alignment of the sequence to the rhoGAP domain (HMM) of at least 8. Preferably, a rhoGAP domain includes at least about 100-250 amino acids, more preferably about 100-200 amino acid residues, or about 140-160 amino acids and has a bit score for the alignment of the sequence to the rhoGAP domain (HMM) of at least 16, 25, 50, 100 or greater. The rhoGAP domain (HMM) has been assigned the PFAM Accession PF00620 ~~(http://pfam.wustl.edu/)~~. An alignment of the rhoGAP domain (amino acids 343-494 of SEQ ID NO:14) of human 33425 with a consensus amino acid sequence derived from a hidden Markov model is depicted in Figure 26.

At pages 44 through 45, please replace paragraphs [0159-160] with the following text:

To identify the presence of an "rhoGAP" domain in a 33425 protein sequence, and make the determination that a polypeptide or protein of interest has a particular profile, the amino acid sequence of the protein can be searched against a database of HMMs (e.g., the Pfam database, release 2.1) using the default parameters ~~(http://www.sanger.ac.uk/Software/Pfam/HMM_search)~~. For example, the hmmsf program, which is available as part of the HMMER package of search programs, is a family specific default program for MILPAT0063 and a score of 15 is the default threshold score for determining a hit. Alternatively, the threshold score for determining a hit can be lowered (e.g., to 8 bits). A description of the Pfam database can be found in Sonhammer et al., (1997) *Proteins* 28(3):405-420 and a detailed description of HMMs can be found, for example, in Gribskov et al., (1990) *Meth. Enzymol.* 183:146-159; Gribskov et al., (1987) *Proc. Natl. Acad. Sci. USA* 84:4355-4358; Krogh et al., (1994) *J. Mol. Biol.*

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235:1501-1531; and Stultz et al., (1993) *Protein Sci.* 2:305-314, the contents of which are incorporated herein by reference.

An additional method to identify the presence of a "RhoGAP" domain in a 33425 protein sequence, and make the determination that a polypeptide or protein of interest has a particular profile, the amino acid sequence of the protein can be searched against a SMART database (Simple Modular Architecture Research Tool, http://smart.embl-heidelberg.de/) of HMMs as described in Schultz *et al.* (1998), *Proc. Natl. Acad. Sci. USA* 95:5857 and Schultz *et al.* (2000) *Nucl. Acids Res* 28:231. The database contains domains identified by profiling with the hidden Markov models of the HMMer2 search program (R. Durbin *et al.* (1998) *Biological sequence analysis: probabilistic models of proteins and nucleic acids.* Cambridge University Press.; http://hmmer.wustl.edu/). The database also is extensively annotated and monitored by experts to enhance accuracy. A search was performed against the HMM database resulting in the identification of a "RhoGAP_3" domain in the amino acid sequence of human 33425 at about residues 340 to 520 of SEQ ID NO:14 (see Figure 24A-C).

At page 45 through 46, please replace paragraphs [0162-0164] with the following text:

A BLAST search was performed against the HMM database resulting in the identification of a region homologous to ProDom family PD301916("Similar NT2RM2000363 cluster Fis FLJ10312 weakly cDNA breakpoint" SEQ ID NO:33, ProDomain Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "Similar NT2RM2000363 cluster Fis FLJ10312 weakly cDNA breakpoint" domain (amino acids 516-608 of SEQ ID NO:14) of human 33425 with a consensus amino acid sequence (SEQ ID NO:33) derived from a hidden Markov model is depicted in Figure 27. The consensus sequence for SEQ ID NO:33 is 39% identical over amino acids 516-608 of SEQ ID NO:14 as shown in Figure 27.

A BLAST search was performed against the HMM database resulting in the identification of a region homologous to ProDom family PD000780("GTPase activating similar GTPase-activating activation domain Fis zinc cDNA subunit" SEQ ID NO:34, ProDomain Release 2001.1; Corpet *et al.* (1999), *Nucl. Acids Res.* 27:263-267 and Gouzy *et al.* (1999) *Computers and Chemistry* 23:333-340 http://www.toulouse.inra.fr/prodom.html). An alignment of the "GTPase activating similar GTPase-activating activation domain Fis zinc cDNA subunit" domain (amino acids 390-486 of SEQ ID NO:14) of human 33425 with a consensus amino acid sequence (SEQ ID NO:34) derived from a hidden Markov model is depicted in Figure 28. The consensus sequence for SEQ ID NO:34 is 36% identical over amino acids 390-486 of SEQ ID NO:14 as shown in Figure 28.

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A BLAST search was performed against the HMM database resulting in the identification of a region homologous to ProDom family PD215173("RLIP" SEQ ID NO:35, ProDomain Release 2001.1; <u>Corpet et al. (1999), Nucl. Acids Res.</u> 27:263-267 and Gouzy et al. (1999) <u>Computers and Chemistry</u> 23:333-340 ~~http://www.toulouse.inra.fr/prodom.html~~). An alignment of the "RLIP" domain (amino acids 399-488 of SEQ ID NO:14) of human 33425 with a consensus amino acid sequence (SEQ ID NO:35) derived from a hidden Markov model is depicted in Figure 29. The consensus sequence for SEQ ID NO:35 is 34% identical over amino acids 399-488 of SEQ ID NO:14 as shown in Figure 29.

At pages 61 through 62, please replace paragraph [0268] with the following text:

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (J. Mol. Biol. (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package ~~(available at http://www.gcg.com)~~, using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package ~~(available at http://www.gcg.com)~~, using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used if the practitioner is uncertain about what parameters should be applied to determine if a molecule is within a sequence identity or homology limitation of the invention) is using a Blossum 62 scoring matrix with a gap open penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

At page 62, please replace paragraph [0270] with the following text:

The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al., (1990) J. Mol. Biol. 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to 80090, 52874, 52880, 63497, or 33425 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to 80090, 52874, 52880, 63497, or 33425 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et

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al., (1997) *Nucleic Acids Res.* 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See ~~http://www.ncbi.nlm.nih.gov.~~